REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

The foregoing amendments were submitted with the response filed August 2, 2010. According to the Advisory Action mailed August 12, 2010, they would not be entered after final. Thus, they are presented again here.

I. Amendments to the Specification

The specification is amended to correct a clerical error in paragraph [0023], relating to the amount of protein used in dose B. Support for the correction is found in Figures 1 and 2 of the specification as filed, which both indicate that 30 μg of NY-ESO-1 protein was used for dose B.

II. Claim Amendments

Claim 20 is amended to recite methods comprising administering an amount of a composition containing full length NY-ESO-1 protein and a saponin based adjuvant that is sufficient to reduce the risk of relapse, wherein the ratio of NY-ESO-1 protein to saponin based adjuvant is about 1:1 by weight. This subject matter is supported in Example 1, which reports the use of compositions comprising NY-ESO-1 protein and saponin based adjuvant (ISCOM) in a ratio of about 1:1 by weight (e.g., 10 μg : 12 μg (dose A); 30 μg : 36 μg (dose B), and 100 μg : 120 μg (dose C)).

Upon entry of this amendment, claims 20-22, 25, 26 and 34-37 will remain pending. These claims are presented for reconsideration.

III. New Matter/Written Description

The Advisory Action mailed August 12, 2010 alleges that the amendments to claim 20 introduce new matter. Specifically, while the Examiner acknowledges two "species" that support this amendment, she questions whether there is support for the claimed "genus."

As set forth in MPEP § 2163.02, "[t]he test for sufficiency of support in a parent application is whether the disclosure of the application relied upon 'reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.'" Importantly, "[t]he subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement."

With regard to written description support for a genus, the MPEP explains that "[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice . . . or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties . . . or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." MPEP § 2163. Further, "[a] 'representative number of species' means that the species which are adequately described are representative of the entire genus." As recognized in the MPEP, "there may be situations where ***one species*** adequately supports a genus." MPEP § 2163 (emphasis added).

Here, the specification discloses ***three*** distinct examples of methods using NY-ESO-1 protein and a saponin based adjuvant where the ratio of NY-ESO-1 protein to saponin based adjuvant is about 1:1 by weight (not just the two cited by the Examiner). Dose A used 10 μg and 12 μg, respectively, Dose B used 30 μg and 36 μg, respectively, while Dose C used 100 μg and 120 μg, respectively. The Advisory Action does not indicate how or why these ***three species*** are insufficient to support the genus of compositions with a "1:1" weight ratio. Indeed, the facts that (i) these three examples differ considerably in the ***amounts*** of components used and (ii) ***all working examples*** of the claimed subject matter used a 1:1 weight ratio as recited in the claims provide strong support for the conclusion that the skilled artisan reviewing the application as filed would have understood that Applicant had possession of methods using NY-ESO-1 protein and saponin based adjuvant in about a 1:1 weight ratio.

Applicant therefore requests favorable reconsideration of the new matter/written description issue.

IV. Indefiniteness

The Advisory Action mailed August 12, 2010 alleges that the amendments to claim 20 raise indefiniteness issues because "Applicant has not redefined the term 'about' in the specification." There is nothing inherently indefinite in the term "about," however, and no general requirement that the term must be expressly defined in the specification.

As set forth in MPEP § 2173.05(b), "[i]n determining the range encompassed by the term "about", one must consider the context of the term as it is used in the specification and claims of the application." Here, the doses that have a mathematical 1:1.2 ratio indicate that "about 1:1" should be interpreted to include 1:1.2. The Office has not indicated why further definition of this claim term is required, or how the context provided by the specification is insufficient to satisfy the minimal, "threshold requirements of clarity and precision" needed to satisfy § 112, second paragraph. Applicant therefore requests favorable reconsideration of the indefiniteness issue, keeping in mind that the claims need only "define the patentable subject matter with a reasonable degree of particularity and distinctness," and must be "analyzed, not in a vacuum, but in light of . . . [t]he content of the particular application disclosure." MPEP § 2173.02.

V. § 102 Rejection

The claims remain rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Cebon *et al.*, *Proc. Amer. Soc. Clin. Oncol.* 21, abstract 86 (June 2002) ("Cebon"). Office Action, at 2-4. Applicant respectfully traverses.

As reflected in independent claim 20, the instant claims are directed to a method for reducing the risk of relapse in a subject at risk of relapse of a cancer, the cells of which express NY-ESO-1, comprising administering to said subject an amount of a composition containing full length NY-ESO-1 protein and a saponin based adjuvant in a ratio of about 1:1 by weight, sufficient to induce an antibody response to NY-ESO-1 in said subject and reduce the risk of relapse.

As explained previously, the cited Cebon abstract does not teach or suggest that a composition containing full length NY-ESO-1 protein and a saponin based adjuvant is able to ***reduce the risk of relapse*** of cancer ***at any dose***. Thus, the Cebon abstract does not describe the claimed invention, or provide any reasonable expectation that administering a composition comprising full length NY-ESO-1 protein and a saponin based adjuvant would be effective to reduce the risk of relapse.

As also explained previously, the cited Cebon abstract does not indicate the amount of ISCOM that was used with the described doses of NY-ESO-1 protein. Thus, the Cebon abstract does not even enable methods of achieving the results it reports, because the skilled artisan seeking to induce the reported "high titre humoral and cellular immune responses" would not know how much ISCOM adjuvant is required to achieve such results. Of course, since Cebon does not even suggest that its compositions might be effective to reduce the risk of relapse, it falls even further short of enabling methods of reducing the risk of relapse.

In the July 12 Advisory Action, the examiner notes that the previously pending claims did not recite an amount of NY-ESO-1 protein or saponin based adjuvant. Applicant does not agree that the claims need to recite specific amounts to overcome the § 102 rejection, because the recitation of an "amount . . . sufficient to . . . reduce the risk of relapse" already distinguishes Cebon, for the reasons outlined above and explained in the previous response. Nevertheless, in order to advance prosecution, Applicant has amended the claims to recite that the administered composition contains "full length NY-ESO-1 protein and a saponin based adjuvant in a ratio of about 1:1 by weight." Because Cebon does not disclose the amounts of ISCOM used with its doses of NY-ESO-1 protein, it does not teach every aspect of the claimed invention as required for a § 102 rejection.

The August 12 Advisory Action states that Applicant's arguments against the §102 rejection "already [were] addressed by the Examiner," but the Office has not addressed the failure of Cebon to teach every aspect of the subject matter recited in the amended claims.

For at least these reasons, Applicant respectfully urges reconsideration and withdrawal of the anticipation rejection based on Cebon.

VI. § 103 Rejections

The claims remain rejected under 35 U.S.C. § 103 for allegedly being obvious in view of (A) WO 98/14464 in view of Batchu (2003) and WO 03/076455; (B) WO 98/14464, Batchu, and WO 03/076455, further in view of Jager (2000) and U.S. 6,506,386; and (C) Cebon, Jager, WO 03/076455 and "an admission in the specification." Applicant addresses these maintained rejections in turn below.

A. WO 98/14464, Batchu (2003) & WO 03/076455

Claims 20-22, 34 and 35 remain rejected over the combination of WO 98/14464, Batchu and WO 03/076455. Applicant respectfully traverses this rejection.

The July 12 Advisory Action maintains this rejection because "Batchu teaches that NY-ESO-1 based therapies can be used . . . to reduce the risk of relapse," but does not provide any citation to support this assertion. As explained previously, Batchu notes that immunotherapeutic approaches using NY-ESO-1 modfied DCs are being ***investigated*** to prevent relapse of aggressive myeloma after chemotherapy ("Discussion," page 1341), but does not teach that its transduced DCs are in fact useful to prevent relapse. Moreover, Batchu provides no indication that a composition comprising NY-ESO-1 and a saponin based adjuvant, rather than NY-ESO-1-modified DCs, would be useful to prevent relapse. Indeed, the assertion that Batchu relates to "NY-ESO-1 based therapies" is misleading, because it generalizes Batchu's teachings where Batchu itself is very specifically related only to the use of NY-ESO-1-modified DCs.

Thus, Applicant reiterates that the combination of WO 98/14464, Batchu and WO 03/076455 does not provide the skilled artisan with any reasonable expectation of success in being able to reduce the risk of relapse by administering a composition containing full length NY-ESO-1 protein and a saponin based adjuvant, as recited in the instant claims. Accordingly, this obviousness rejection is improper and should be withdrawn.

The August 12 Advisory Action states that Applicant's arguments in this section "already have been addressed," but the Office has not acknowledged the fact that Batchu does

not teach that its "NY-ESO-1 based therapies" are effective to reduce the risk of relapse, and has not established how the cited combination of references provides any reasonable expectation of success in such an unpredictable field as reducing the risk of cancer relapse.

B. WO 98/14464, Batchu, WO 03/076455, Jager and U.S. 6,506,386

Claims 25, 26, 36 and 37 are rejected over the combination of WO 98/14464, Batchu WO 03/076455, Jager and U.S. 6,506,386. Applicant respectfully traverses this rejection.

In maintaining this rejection, the Advisory Action again relies on Batchu for teaching that immune responses can reduce the risk of relapse. As discussed above, however, Batchu's teachings do not go this far, and its unsupported speculations do not enable any methods of reducing the risk of relapse, let alone methods using NY-ESO-1 protein (as claimed) instead of NY-ESO-1-modified DCs.

The July 12 and August 12 Advisory Actions criticize Applicant for arguing Jager "separately," rather in view of Batchu and the other cited references. But, Jager is the only reference that uses NY-ESO-1 peptides *per se* in immunotherapeutic methods. Thus, Jager's reported results, which ***do not show any prevention of relapse***, are indeed pertinent to the pending rejection. The skilled artisan reviewing Jager, and seeing that 4/5 responsive patients ***developed additional lesions*** after vaccination with NY-ESO-1 protein, certainly would not have expected to be able to reduce the risk of relapse by administering an NY-ESO-1 protein-containing composition, as claimed. Certainly, Batchu's theoretical and speculative comments would not have overridden the expectations arising from the actual results reported in Jager.

The August 12 Advisory Action states that Applicant has not pointed to the portion of Jager that discusses the development of additional lesions in 4/5 originally responsive patients. Applicant notes that this aspect of Jager first was discussed at page 9 of the Response filed June 25, 2010, where Applicant cited page 12201, col. 2, of Jager. This portion of Jager discusses the patient results in detail, with new lesions noted in patients NW415, NW836, NW 46, and NW731. Page 12203, col. 2, also discusses the subsequent

"disease progression" in patients NW415, NW836, and NW 46 "despite [initial] disease stabilization and strong CD8+ T-cell and DTH reactivity."

The August 12 Advisory Action states that "Jager et al. differentiate the antibody-negative patients from the antibody-positive patients, and 5/7 of the patients in the former group developed stabilization or regression of individual metastases." According to the Examiner, this provides "evidence of a reasonable expectation of success in producing the claimed invention." What the Examiner has failed to appreciate is that it is ***this same patient population***, e.g., patients that initially "developed stabilization or regression of individual metastases" that ***developed new lesions*** during the course of Jager's study. Thus, contrary to providing any expectation of success, the results reported in Jager underscore the unpredictability in this field, and demonstrate that initial patient responses are not, in fact, correlated with reducing the risk of relapse. When Jager is reviewed in its entirety, as it must be when assessing obviousness, it is clear that it does not support the rejection for at least these reasons.

Thus, Applicant stands by its position that the combination of WO 98/14464, Batchu, WO 03/076455, Jager and U.S. 6,506,386 does not render obvious the claimed methods. Accordingly, Applicant respectfully urges reconsideration and withdrawal of this § 103 rejection.

C. Cebon, Jager, WO 03/076455 & "the specification"

Claims 20-22, 25, 26 and 34-37 remain rejected over the combination of Cebon, Jager, WO 03/076455, Jager and an alleged "admission" in the specification regarding the patient population studied to evaluate the risk of relapse. Applicant respectfully traverses this rejection.

As explained previously, this rejection is founded on the incorrect assumption that Cebon teaches the amounts of NY-ESO-1 protein and saponin-based adjuvant recited in the claims, which it does not. Moreover, as explained above with reference to the § 102 rejection, the instant claims are even further distinguished from Cebon. Combining Cebon with Jager and WO 03/076455 fails to remedy its deficiencies. As shown above, Jager does

not provide any expectation of success with regard to the ability to reduce the risk of relapse. Indeed, no combination of Cebon, Jager and WO 03/076455 provides any indication that any amount of NY-ESO-1 protein and saponin-based adjuvant would be effective to reduce the risk of relapse. Thus, this combination of references fails to establish a prima facie case of obviousness. Applicant therefore respectfully urges reconsideration and withdrawal of this § 103 rejection.

The August 12 Advisory Action states that Applicant's arguments in this section were "previously responded to," but the Office has not reconsidered the rejection in view of the amended claims, or the shortcomings of Batchu and Jager discussed above.

VII. Unexpected Results

The July 12 Advisory Action dismissed Applicant's evidence of unexpected results for two reasons, neither of which are valid. (The August 12 Advisory Action largely incorporates the same rationale.)

First, the July 12 Advisory Action alleged that "the art references shows the same result, so the result is not unexpected." This is simply not true. None of the cited references report any results showing a method that is effective to reduce the risk of relapse of an NY-ESO-1-expressing cancer, as recited in the instant claims.

- Cebon presents only initial immunological data, with ***no clinical results whatsoever***, let alone long-term results such as a reduction in relapse.
- Batchu ***speculates*** that NY-ESO-1-modified DCs might have the ***potential*** to generate CTLs that might, in turn, be effective to eliminate residual myeloma cells responsible for relapse, but notes that results obtained to date with gene-modified DCs "are far from satisfactory." (*See* page 1341, col. 2)
- Jager reports that 4/5 responsive patients ***developed additional lesions*** after vaccination.

Thus, the results reported in Example 6 of the instant specification and in the further follow-up study reported in the Nicholaou manuscript submitted previously, showing a significant reduction in the risk of relapse, indeed are surprising and unexpected.

Second, the July 12 Advisory Action noted that "the claims do not recite that the risk of relapse is reduced for the length of time that Applicant asserts is unexpected." However, there is no requirement that the claims expressly recite the unexpected results achieved by the claimed invention in order for the unexpected results to support patentability. This issue was addressed by the Federal Circuit in a decision that is binding on the Patent Office, *In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007) (reversing a Board decision on obviousness where the Board failed to consider evidence of unexpected results). The court explained that "[t]he issue . . . is not whether a claim ***recites*** a new use, but whether the subject matter of the claim ***possesses an unexpected use***." *Id.* at 1353 (emphasis added).

The August 12 Office Action states that "Applicant is arguing an unrecited limitation in 'long-term.'" First, as noted above, precedential case law that is binding on the Patent Office holds that unexpected results cited in support of non-obviousness need not be recited in the claims, as long as they pertain to the claimed subject matter, which they do here. Moreover, Applicant notes that the claim language itself— reducing the risk of relapse— connotes a long-term effect. Thus, the unexpected results fully support the pending claims.

As shown previously, the claimed methods possess an unexpected use—the ability to reduce the risk of relapse of NY-ESO-1-expressing cancer. Because none of the cited references teach or suggest a method for preventing relapse of NY-ESO-1-expressing cancer, nor indicate that the claimed methods would achieve such dramatic, long-term, beneficial results in the context of preventing relapse, the results reported in the instant application and Nicholaou indeed are evidence of unexpected results that further support patentability.

For at least these reasons, Applicant respectfully urges reconsideration and withdrawal of the obviousness rejections.

VIII. Request for Information Under 37 CFR § 1.105

The August 12 Advisory Action acknowledges the response to the Request for Information under 37 CFR § 1.105. However, the Examiner states that the two new sets of slides "have been noted by the Examiner, but they have not been considered on the Form 1449" because the number of pages was not indicated. Applicant submits herewith a revised set of slides with ***page numbers added for the Examiner's convenience***, along with a new SB/08 to be initialed. Applicant emphasizes that the page numbers were not present on the original slides, and thus does not understand the basis for the refusal to consider them.

Conclusion

Applicant believes that the present application is now in condition for allowance, and favorable reconsideration thereof is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date September 29, 2010 By _____

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